## AMENDMENTS TO THE SPECIFICATION

On page 1, between paragraphs [1] and [2], kindly insert the following paragraph:

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

[01.1] The research for this invention was supported in part by funds from the U.S. government. The U.S. government may therefore have certain rights in the invention.

On page 3, in the BRIEF DESCRIPTION OF THE DRAWINGS, before paragraph [12], kindly insert and amend the following paragraphs:

[11.1] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawings will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

[11.2] FIG. 1 shows two models of solid tumor heterogeneity. In the classic model (FIG. 1A), mutations or environmental differences cause tumor cells to adopt a variety of different phenotypes. Environmentally determined differences in phenotype, represented by white, green, and red cells, may be reversible while mutationally determined changes in phenotype, represented by purple cells, may not be reversible. Many cells with a variety of different phenotypes are thought to have the potential to proliferate extensively and form new tumors. The tumor stem cell model (FIG. 1B) is distinguished by having only a minor population of tumor cells that are tumorigenic (yellow cells). These tumor stem cells are characterized by indefinite proliferative potential, the ability to form new tumors, and the ability to give rise to heterogeneous non-tumorigenic cancer cells that typically form the bulk of a tumor.

On page 134, kindly amend the Abstract to be a single paragraph, as follows:

ABSTRACT

A small percentage of cells within an established solid tumor have the properties of stem cells. These solid tumor stem cells give rise both to more tumor stem cells and to the majority of cells in the tumor that have lost the capacity for extensive proliferation and the ability to give rise to new tumors. ~~Thus,~~ The solid tumor heterogeneity reflects the presence of tumor cell progeny arising from a solid tumor stem cell. This discovery is the basis for solid tumor stem cell

compositions, methods for distinguishing functionally different populations of tumor cells, methods for using these tumor cell populations for studying the effects of therapeutic agents on tumor growth, and methods for identifying and testing novel anti-cancer therapies directed to solid tumor stem cells.

~~We have developed a xenograft model in which we have been able to establish tumors from primary tumors via injection of tumors in the mammary gland of severely immunodeficient mice. Xenograft tumors have been established from mastectomy specimens of breast cancer patients. Furthermore, in the three tumors that we have tested, we have been able to make single-cell suspensions and transfer the tumors serially through immunocompromised mice. These improvements in the xenograft assay have allowed us to do biological and molecular assays to characterize clonogenic solid tumor stem cells.~~

~~We have also developed evidence that strongly implicates the Notch pathway, especially Notch 4, as playing a central pathway in carcinogenesis. Antibodies against Notch4 reduced tumor cell proliferation and survival.~~